Alcohol Withdrawal Hallucinations in the General Population, an Epidemiological Study

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Abstract

Hallucinations are sometimes encountered in the course of alcohol withdrawal; however, both the factors predisposing to alcohol withdrawal hallucinations (AWH) and the implications of AWH with respect to the mechanisms of hallucinations remain unclear. To clarify these issues, we used data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) to investigate the demographic correlates, alcohol-use clinical patterns, and psychiatric comorbidities in two groups: drinkers with and without a history of AWH. We estimated the odds ratios for studied factors and used logistic regression analyses to compare the two groups. We found that over 2% of drinkers reported AWH (758 of a sample of 34,533 subjects). Alcohol tolerance and withdrawal seizures were highly associated with AWH, and exposure to alcohol during brain development was associated with a 10-fold increase in AWH compared to

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exposure during adulthood. African Americans, Native Americans, and unmarried subjects, as well as subjects with lower levels of education and lower levels of income were more likely to experience AWH. Furthermore, those with a history of AWH had higher odds ratios for most psychiatric illnesses than those without such history—yet of anxiety disorders, only panic was associated with AWH. These associations suggest that higher levels of education and of standard of living could protect against AWH; while social isolation, hypervigilance, exposure to alcohol during brain development, and long and severe exposure to alcohol could predispose to AWH.

1. Introduction

Hallucinations refer to experiences whereby perceptions are devoid of external stimuli (Esquirol, 1817). Originally considered pathognomonic for illnesses such as schizophrenia, they are encountered in many psychiatric, neurological and general medical conditions as well as the general population (Stephane et al., 2015). Hallucinations associated with alcohol use have been described for over a century (Kraepelin, 1913; Marcel, 1847).

In the context of alcohol use , hallucinations can occur during alcohol intoxication, alcohol withdrawal, or after intoxication and withdrawal (Johanson, 1961; Tsuang et al., 1994). Although alcohol related hallucinations is not associated with elevated family incidence of schizophrenia(Schuckit and Winokur, 1971; Tsuang et al., 1994), it could convert to a psychotic illness in 5% of the cases (Niemi-Pynttäri et al.,

2013). Furthermore, alcohol-associated hallucinations may occur in the context of a clear or clouded sensorium, and in association with other psychotic symptoms (such as delusions and anosognosia "i.e. lack of insight") or without associated psychotic symptoms. It appears that, just like hallucinations could occur through a combination of mechanisms(Stephane, 2013), alcohol can cause hallucinations through multiple routes.

By investigating the demographic and clinical features of alcohol-associated hallucinations, epidemiological studies could not only provide useful information regarding the treatment for patients with alcohol use disorder but, also shed light about the routes through which alcohol causes hallucinations and about the mechanisms of hallucinations in general.

Many studies have examined the demographics and comorbidities of alcohol-induced psychotic disorder (AIPD) and of alcohol-induced hallucinations (AIH), using criteria consistent with DSM-5 ((APA), 2013) and ICD-10((WHO), 1993) definitions. Both the DSM-5 and ICD-10 define AIPD as the occurrence of hallucinations or delusions not accounted for by another psychotic disorder during alcohol *intoxication* or *withdrawal from alcohol or within a month of use or withdrawal*. As alcohol affects the brain differently during these distinct time frames--intoxication, withdrawal and post withdrawal--it is important to account for the temporal relationship between hallucinations and alcohol use in order to further understand the mechanisms and treatment of alcohol-associated hallucinations. In other words, the factors that predispose for hallucinations during intoxication may not be the same as those that predispose for hallucinations during withdrawal. Additionally, the vast majority of these

studies involved clinical populations and reported variable findings depending on the patient populations under study and the country where the study was carried out (Jordaan and Emsley, 2014; Schuckit, 1982; Sedain, 2013; Soyka, 2008; Tsuang et al., 1994). This focus on clinical populations could constitute a selection bias and blur findings, as drinkers who experience hallucinations may not necessarily seek clinical care. In this regard, the study of the general population could provide more accurate estimates of the factors related to alcohol-associated hallucinations.

Given these considerations, we focus in the present study on Alcohol Withdrawal Hallucinations (AWH) in the general population (and exclude hallucinations that occur during the use of alcohol or after withdrawal from alcohol). AWH is one of many symptoms suggestive of central and autonomous nervous systems hyper-excitability that could occur during Alcohol withdrawal; these include tremor, fever, autonomous instability and seizures(Heilig et al., 2010). AWH involve visual, auditory, tactile, taste and olfactory sensory modalities, in order of frequency(Deiker and Chambers, 1978); as such, AWH are distinguishable from hallucinations encountered in schizophrenia where auditory verbal hallucinations are prominent (Stephane et al., 2003). We investigate the prevalence and the demographic correlates of AWH, as well as alcohol use patterns and psychiatric comorbidity. To avoid over-estimation of these factors, we use data from the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)which include a large sample of drinkers from the general population (34,533 subjects). To our knowledge, there is no prior epidemiological research that specifically examined AWH in a nationally representative sample in the U.S or other countries. We

hypothesize that understanding of the demographics, alcohol use patterns, and psychiatric comorbidity associated with AWH would shed light on the pathogenesis of AWH that could impact both treatment and future research.

2. Methods

2.1. Subjects

The study used data from Wave 1 of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC)—a 2001-2002 survey of a nationally representative sample of noninstitutionalized adults in the United States. The nationwide survey was conducted with 43,093 participants aged ≥ 18 years in face-to-face household setting by the US Census Bureau. The details of the sampling methods and study procedures used for the NESARC are described elsewhere (Grant et al., 2004). The survey provides data primarily on alcohol consumption and alcohol use disorders. In addition, the survey includes data on sociodemographic variables, classification of psychiatric disorders, treatment utilization, and medical conditions. The NESARC was sponsored and designed by the National Institute on Alcohol Abuse and Alcoholism. The NESARC procedures were reviewed and approved by the US Census Bureau and the US Office of Management and Budget. Informed consent was obtained from all NESARC participants.

Of the 43,093 adults in the NESARC, 34,533 drinkers (80.1%) were included for data analysis after excluding 8,266 lifetime alcohol abstainers and 294 individuals who did not know their status of AWH. The presence of lifetime AWH was assessed by face-

to-face interviews with the following questions: “The next few questions are about the bad aftereffects of drinking that people may have when the effects of alcohol are wearing off. This includes the morning after drinking or in the first few days after stopping or cutting down. Did you ever see, feel, or hear things that weren’t really there when the effects of alcohol were wearing off?” Possible responses included "Yes," "No," and "Don't know". Based on their responses, subjects were divided in two groups: (1) with AWH and (2) without AWH.

2.2. Outcome measures

2.2.1. Demographics

The following demographic variables were obtained on each subject: gender, race/ethnicity, age, level of education, marital status, and personal income.

2.2.2. Alcohol use patterns

Subjects provided information about the following alcohol use history: age at the first alcoholic drink, age of onset of alcohol dependence, number of episodes of alcohol dependence, duration of the longest episode of alcohol dependence, alcohol tolerance, and alcohol withdrawal seizures.

2.2.3. Comorbid psychiatric disorders

The Alcohol Use Disorder and Associated Disabilities Interview Schedule–DSM-IV Version (AUDADIS-IV) was administered to diagnose lifetime psychiatric disorders

(except psychotic disorders) (Grant et al., 2003). The AUDADIS-IV has demonstrated fair-to-good reliability for lifetime psychiatric disorders as follows: alcohol abuse and dependence (kappa 0.70), tobacco dependence (kappa 0.60), major depressive disorder (kappa 0.65), dysthymia (kappa 0.58), anxiety disorders (kappa = 0.42 to 0.48), and personality disorders (kappa = 0.42 to 0.67) (Grant et al., 2003). Psychotic disorders were considered comorbid whenever participants reported a prior diagnosis by a physician and/or other health professional of schizophrenia, a psychotic illness or a psychotic episode.

The current study, therefore, includes data about lifetime comorbidity of the following psychiatric disorders: (1) substance use disorders (alcohol abuse/dependence, drug abuse/dependence, and nicotine dependence); (2) mood disorders (major depressive disorder, dysthymic disorder, mania, and hypomania); (3) anxiety disorders (panic disorder without agoraphobia, panic disorder with agoraphobia, agoraphobia without a history of panic disorder, social phobia, specific phobia, and generalized anxiety disorder); (4) personality disorders (histrionic, antisocial, avoidant, paranoid, schizoid, obsessive-compulsive, and dependent personality disorder); (5) psychotic disorders; and (6) pathological gambling. Of note, the diagnoses of mood and anxiety disorders excluded illness-induced or substance-induced mood and anxiety disorders.

2.3. Statistical Analyses

Statistical analyses were carried out with SPSS Version 19 (IBM SPSS; Armonk, New York). Based on the presence or absence of AWH, we first divided participants into two groups: with AWH and without AWH. We subsequently cross-tabulated the data and

computed the rates and odds ratios (OR) of the demographic variables, lifetime alcohol-related clinical patterns, and lifetime comorbid psychiatric disorders. The differences in psychiatric comorbidity between the two groups were estimated using OR at a 99% confidence intervals. The group differences with respect to the demographic variables and alcohol-related clinical patterns were estimated using OR and logistic regression analyses. For the analysis of demographic variables, we estimated both unadjusted odds ratios (OR) and adjusted odds ratios (AOR) by using alcohol-related clinical covariates (age at first alcoholic drink, age at onset of alcohol dependence, number of episode of alcohol dependence, and duration of longest episode of alcohol dependence).

To address the multiple comparisons problem and the possibility of type II error, we used a 99% confidence interval instead of a 95% interval. Furthermore, for the analysis of lifetime psychiatric comorbidity (Table 3), we first estimated unadjusted odds ratios (OR) and 99% confidence intervals. Second, we estimated adjusted odds ratios (AOR) and 99% confidence intervals adjusting for demographic covariates (gender, race, age, education, marital status, and personal income). Third, we estimated the odds ratios (AOR) while adjusting for both the demographic variables (gender, race, age, education, marital status, and personal income) and psychiatric disorders (any substance use disorder, any mood disorder, any anxiety disorder, and any personality disorder).

Adjustment for demographic variables and psychiatric comorbidity was carried out by including these factors as covariates in the logistic regression analyses. In the case of psychiatric comorbidity, conditions other than ones of interest (regressed) were

included as covariates. Thus, each mood disorder was adjusted for any substance use disorder, any anxiety disorder, and any personality disorder. Each anxiety disorder was adjusted for any substance use disorder, any mood disorder, and any personality disorder. Each personality disorder was adjusted for any substance use disorder, any mood disorder, and any anxiety disorder. Each substance use disorder was adjusted for any mood disorder, any anxiety disorder, any personality disorder, and all other substance use disorders (except the same substance abuse/dependence).

3. Results

3.1. Demographic Characteristics associated with AWH

The lifetime prevalence of AWH in this sample was 2.2%, with 758 subjects having history of AWH and 34,533 subjects without AWH history. Table 1 details the demographic differences between the two groups. Males and subjects over 65 were about twice as likely to develop AWH relative to females and younger subjects, respectively. AWH were also more frequent in African American and Native American subjects relative to Asian, Caucasian, and Hispanic subjects. We also found that higher level of education and higher level of income were associated with lower likelihood of AWH (Figure 1). Marital status also affected the relative risk for AWH. Relative to those living as couples (married/cohabitation), subjects who were divorced or separated have the highest rate of AWH and those who were never married have the second highest. Widowed individuals did not differ from married ones in the rate of AWH.

Adjusting for alcohol related clinical patterns (age at first alcoholic drink, age at onset of alcohol dependence, number of episode of alcohol dependence, and duration

of longest episode of alcohol dependence), the factors of race, level of education, level of income, and marital status remained significant but not the age or gender factors. With respect to marital status divorced/separated and widowed, but not never married, were significant.

3.2. Alcohol-related clinical patterns

A history of alcohol withdrawal hallucinations was significantly associated with younger age at first alcoholic drink, onset of alcohol dependence at age 17 or younger, duration of the longest episode of alcohol dependence of 37 months or longer, development of alcohol tolerance, and history of withdrawal seizure. Remarkably, those with a history of AWH had 16.53 times greater odds of alcohol tolerance (99% CI 12.77-21.38) and 56.45 times greater odds of alcohol withdrawal seizures (99% CI 38.76-82.21), relative to subjects without AWH history. Table 2 and Figure 2 provide details of these findings.

3.3. Lifetime Comorbid Psychiatric Disorders

Logistic regression analysis showed that a history of AWH was significantly associated with all six diagnostic categories of psychiatric disorders (any substance use disorder, any mood disorder, any anxiety disorder, any personality disorder, psychotic disorders, and pathological gambling), and with all specific disorders under each category. ORs remained significant for all disorders after adjusting for demographic variables. However, adjusting for demographic variables and other psychiatric disorders, the association of AWH with alcohol abuse, hypomania, any anxiety disorder, and most of

the specific anxiety disorders (other than panic disorder with or without agoraphobia) became insignificant. Table 3 provides details of these results. Not included in table three, further adjustment for the length and severity of alcohol use had minimal effects on the results.

4. Discussion

Hallucinations, as expected, are hardly specific to psychotic illnesses. Our data show over 2.2% lifetime prevalence of AWH in the general population—a prevalence twice as high as that of schizophrenia(van Os and Kapur, 2009), and about third of that of all psychotic disorders combined(Perälä et al., 2007). The prevalence of AWH, however, is lower than that of hallucinations in the general population. A British epidemiological study on a sample of 8580 participants found an annual prevalence of 4.2% of visual and/or auditory hallucinations(Johns et al., 2004). These findings indicate that psychotic illnesses and alcohol withdrawal are few of multiple pathological entities that could lead to experiencing hallucinations. It appears that as far as pathogenesis, just like fever or headache, hallucinations are not a specific symptom (Stephane et al., 2015).

To our knowledge this is the first epidemiological study that specifically examined AWH in the general population. A previous study in Finland by Perälä and colleagues has examined AIPD in the general population, and reported a lifetime prevalence of 0.5% (Perälä et al., 2010). However, AIPD and AWH are not synonymous, the first refers to a condition whereas the second refers to symptoms that occur during

a condition, alcohol withdrawal. Furthermore, Perälä et al employed stringent inclusion criteria; subjects were included only when hallucinations were in excess of those usually associated with alcohol intoxication or withdrawal with perceptual disturbances, were severe enough to warrant clinical attention, and lasting for a minimum of one day. It should be also noted that wide range of variability of the prevalence of AIH and of AIPD has been reported in populations of drinkers seeking psychiatric care. A prevalence rate of 0.4-0.7% among inpatient population in Germany (Soyka, 2008), 7.5% among patient in a rehabilitation program in the United States (Tsuang et al., 1994), 12.36% among outpatients in Nepal(Sedain, 2013), and 43% among outpatients in the US (Schuckit, 1982) were reported for either AIH or AIPD.

In line with the unspecificity of hallucinations as a symptom of disease, we show that AWH have significant comorbidity with the vast majority of diagnostic categories of mental illness, and these findings are consistent with the above mentioned epidemiological study (Perälä et al., 2010) and with other studies that examined populations of drinkers seeking clinical care(Tsuang et al., 1994). While in an epidemiological study like ours, comorbidity reflects association rather than concomitance, this association indicates predisposition to a wide range of psychopathology in subjects with AWH. Therefore, it is necessary to carry out a comprehensive screening for psychopathology when these subjects seek clinical care. A treatment for hallucinations as a symptom of psychosis may fall short of appropriate treatment for these subjects. In fact, our data shows that co-morbidity of psychosis was not any higher than that of other psychopathologies.

Psychiatric comorbidity in this study were informative in another aspect. Of the anxiety disorders, only those involving panic were comorbid with AWH. This association might be related to a predisposition to hypervigilance (attentiveness to bodily sensations) in patients with panic disorder (Tull et al., 2008). Hypervigilance has been previously implicated in the etiology of hallucinations in general (Garwood et al., 2015).

Our study also demonstrates associations between AWH and a number of outcome measures that could be predisposing or protective factors for AWH. As can be seen in Figure 1, there is a strong association between the age at first drink and the development of AWH—the earlier alcohol consumption starts the more likely AWH become. Interestingly, the likelihood to develop AWH when drinking commences before age 14 years is 10 times higher than when it starts in early adulthood. This likely reflects the effects of alcohol on brain development as well as the effects of a longer brain exposure to alcohol with the earlier onset of drinking habit. Suggestive of the latter possibility, is the high association of AWH with the severity of alcohol use, as evidenced by both alcohol dependence and alcohol withdrawal seizures.

In contrast to the above, a higher level of education and a higher income had lesser associations with AWH (Figure 2). These effects were independent from the severity and length of alcohol use, which suggests that higher education and higher living standard protect against AWH, possibly due to better brain maturation associated with these factors. Although moderate genetic correlation was reported between alcohol dependence and aspects of impaired cognitive ability (poor verbal capacity as measured by the vocabulary subtest of the Wechsler Adult Intelligence Scale - Revised

(WAIS-R))(Latvala et al., 2011), our study shows that the lesser associations of higher education and better life circumstances with AWW were independent from alcohol dependence and, as such, are likely independent from the genes poor for both alcohol dependence and impaired verbal capacity. Although a precise mechanism cannot be suggested from our data, the potential effects of education and life circumstances on AWH appear to take place through epigenetic routes.

Our study also shows that controlling for the severity and length of alcohol use, there was no gender or age differences with respect to the association with AWH. However, higher association with AWH persisted in Native Americans and African American relative to Asians, Caucasians and Hispanics. The finding could indicate genetic differences in the predisposition to AWH. Interestingly, these demographic correlates of AWH were not found when studies examined populations seeking clinical care(Sedain, 2013; Soyka, 2008).

An interesting finding in our study involves the association patterns of AWH with marital status. Taking in account alcohol use severity and length, divorced/separated/widowed people were about twice as likely to report AWH than those who live in couples. This could be related to the possibility that Divorced/separated/widowed persons are likely to be predisposed for factors implicated in the pathogenesis of non-substance related hallucinations such as social withdrawal (Arieti, 1974; Hoffman, 2008), sensory deprivation (such as in Charles Bonnet Syndrome) (Pang, 2016), and stress(Geddes et al., 2016). Our findings suggest that alcohol withdrawal might augment the effects of these factors and results in AWH.

Conclusions

AWH are highly common in the general population and are more likely to occur when alcohol exposure starts during brain development, and when exposure is severe and prolonged. AWH are also more likely to occur in the context of social isolation, sensory deprivation, stress, and hypervigilance; these are factors that have been implicated in the pathogenesis of non-substance related hallucinations. Higher education and higher income as well as living in couples appear to protect against the development of AWH possibly by stabilizing the neural circuits activated during alcohol withdrawal. AWH were found to be comorbid with a vast array of psychiatric conditions, which supports the notion that hallucinations are general non-disease-specific symptoms.

Our findings and conclusions should be understood in context of cross sectional studies and of the limitations inherent to epidemiologic surveys. The reported associations suggest, but do not confirm, causation. Furthermore, self-report (here, of psychosis)usually has good specificity but low sensitivity(Perälä et al., 2007), and is limited by factors such as recall bias, lack of laboratory markers, and lack of validity measures(Stephane et al., 2006). Additionally, the survey investigated AWH irrespective of the sensory modality of the hallucinations, provided minimal information about hallucinations and did not address the characteristics of hallucinations in each modality. As many of the neural correlates of hallucinations depend on the sensory modality as well as the characteristics of hallucinations, future research that takes in account these factors is needed. Furthermore, future research that compares clinical and demographic factors in subgroups defined depending on the chronological relationship between

hallucinations and alcohol use (intoxication, withdrawal, and post withdrawal) could provide important information about the different pathways for alcohol-related hallucinations.

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Figure 1 Relationship between the Age at first drink and odds Ratio of developing AWH

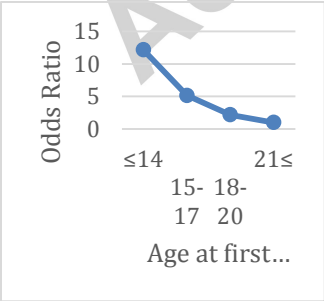
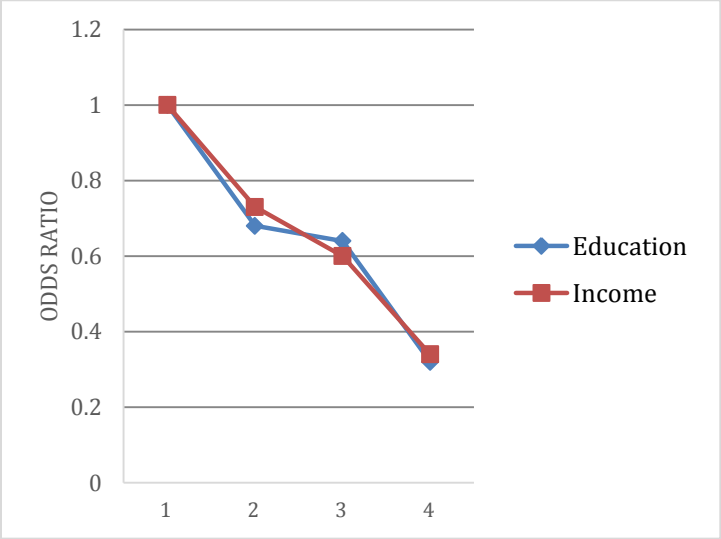


Figure 2. Relationship between Education and Income levels and Odds Ratio for developing AWH.



Education level (in years): 1= 0-11, 2 = 12 , 3= 13-15, and 4= 16 years or more.

Income level (in dollars): 1 = 0-19,999; 2= 20,000-34,999; 3 = 35,000-59,999; 4= 60000 $ or more

Table *1*. Demographic characteristics of drinkers with and without alcohol withdrawal hallucinations.

	Alcohol Withdrawal Hallucinations				
	Yes	No			
Characteristics	(n = 758)	(n = 33,775)	OR (99% CI)	AOR[a] (99% CI)	AOR[b] (99% CI)
Gender					
Male	475 (62.7%)	15637 (46.3%)	**1.95 (1.60-2.37)**	0.97 (0.76-1.25)	0.96 (0.74-1.24)
Female	283 (37.3%)	18138 (53.7%)	1 (Reference)	1 (Reference)	1 (Reference)
Race/Ethnicity					
White	405 (53.4%)	20507 (60.7%)	1 (Reference)	1 (Reference)	1 (Reference)
Black	166 (21.9%)	5970 (17.7%)	**1.41 (1.11-1.79)**	**2.37 (1.71-3.27)**	**2.40 (1.72-3.35)**
Native American	29 (3.8%)	552 (1.6%)	**2.66 (1.60-4.42)**	**2.54 (1.42-4.51)**	**2.51 (1.37-4.60)**
Asian/Pacific Islander	9 (1.2%)	815 (2.4%)	0.56 (0.23-1.34)	0.92 (0.33-2.59)	0.99 (0.35-2.77)
Hispanic	149 (19.7%)	5931 (17.6%)	1.27 (0.99-1.63)	1.33 (0.95-1.88)	1.44 (1.00-2.07)
Age (years)					
18-29	150 (19.8%)	6725 (19.9%)	1 (Reference)	1 (Reference)	1 (Reference)
30-44	272 (35.9%)	11020 (32.6%)	1.11 (0.85-1.44)	1.29 (0.93-1.80)	0.91 (0.64-1.29)

45-64	271 (35.8%)	10359 (30.7%)	1.17 (0.90-1.53)	**2.25 (1.58-3.20)**	1.27 (0.89-1.82)
65 or older	65 (8.6%)	5671 (16.8%)	**0.51 (0.35-0.76)**	**3.03 (1.77-5.18)**	1.41 (0.81-2.45)
Education (years)					
0-11	185 (24.4%)	5136 (15.2%)	1 (Reference)	1 (Reference)	1 (Reference)
12	235 (31.0%)	9616 (28.5%)	**0.68 (0.53-0.88)**	**0.66 (0.47-0.93)**	**0.60 (0.42-0.86)**
13-15	239 (31.5%)	10449 (30.9%)	**0.64 (0.49-0.82)**	**0.54 (0.38-0.75)**	**0.51 (0.36-0.72)**
16 or more	99 (13.1%)	8574 (25.4%)	**0.32 (0.23-0.44)**	**0.27 (0.17-0.41)**	**0.25 (0.16-0.39)**
Marital status					
Married/cohabitation	336 (44.3%)	17799 (52.7%)	1 (Reference)	1 (Reference)	1 (Reference)
Divorced/separated	198 (26.1%)	5595 (16.6%)	**1.88 (1.48-2.37)**	**1.69 (1.25-2.29)**	**1.61 (1.17-2.20)**
Never married	187 (24.7%)	7615 (22.5%)	**1.30 (1.03-1.65)**	0.84 (0.62-1.14)	1.09 (0.79-1.50)
Widowed	37 (4.9%)	2766 (8.2%)	0.71 (0.45-1.11)	**2.50 (1.38-4.60)**	**2.15 (1.16-4.00)**
Personal income ($)					
0-19999	431 (56.9%)	15002 (44.4%)	1 (Reference)	1 (Reference)	1 (Reference)
20000-34999	173 (22.8%)	8250 (24.4%)	**0.73 (0.58-0.92)**	**0.61 (0.45-0.82)**	**0.55 (0.40-0.76)**
35000-59999	116 (15.3%)	6681 (19.8%)	**0.60 (0.46-0.79)**	**0.49 (0.34-0.69)**	**0.45 (0.31-0.65)**
60000 or more	38 (5.0%)	3842 (11.4%)	**0.34 (0.22-0.53)**	**0.29 (0.17-0.51)**	**0.25 (0.14-0.45)**

Abbreviations: OR, odds ratio; CI, confidence interval. Bold font indicates statistical significance

[a] Adjusted for age at first alcoholic drink and age at onset of alcohol dependence

[b] Adjusted for number of episode of alcohol dependence and duration of longest episode of alcohol dependence

Table *2*. Lifetime alcohol-related clinical correlates among drinkers with and without alcohol withdrawal hallucinations.

	Alcohol Withdrawal Hallucinations		
	Yes	No	
Characteristics	(n = 758)	(n = 33,775)	OR (99% CI)
Age at first alcoholic drink (years)			
14 or younger	27.1%	7.2%	**12.16 (8.56-17.27)**
15-17	37.9%	23.7%	**5.15 (3.69-7.20)**
18-20	24.9%	36.4%	**2.20 (1.55-3.14)**
21 or older	10.1%	32.6%	1 (Reference)
Age at onset of AD (years)*			
17 or younger	21.2%	12.8%	**1.71 (1.18-2.47)**
18-20	26.7%	30.1%	0.91 (0.65-1.28)

21-24	18.1%	22.0%	0.84 (0.58-1.23)
25-29	11.6%	12.2%	0.97 (0.63-1.50)
30 or older	22.4%	23.0%	1 (Reference)
Number of episode of AD*			
1	69.2%	72.9%	1 (Reference)
2	12.8%	12.7%	1.06 (0.73-1.55)
3	6.9%	6.3%	1.15 (0.70-1.90)
4 or more	11.1%	8.1%	1.48 (0.96-2.18)
Duration of longest episode of AD (months)*			
1-6	32.4%	43.4%	1 (Reference)
7-12	10.5%	14.7%	0.95 (0.62-1.46)
13-36	18.1%	19.4%	1.25 (0.88-1.79)
37-60	11.5%	9.1%	**1.69 (1.11-2.57)**
61 or longer	27.6%	13.4%	**2.76 (2.00-3.81)**
Alcohol tolerance			
No	16.0%	75.8%	1 (Reference)
Yes	84.0%	24.2%	**16.53 (12.77-21.38)**
Alcohol withdrawal seizure			
No	86.0%	99.7%	1 (Reference)
Yes	14.0%	0.3%	**56.45 (38.76-82.21)**

Abbreviations: AD, alcohol dependence; OR, odds ratio; CI, confidence interval. Bold font indicates significance.

* Alcohol dependence was present in 67.8% of AWH group and 12.6% of non-AWH group, the percentages were computed with individuals with alcohol dependence in each group separately.

Table *3.* Lifetime Prevalence rates and adjusted odds ratios of comorbid psychiatric disorders among drinkers with and without alcohol withdrawal hallucinations.

	Alcohol Withdrawal Hallucinations	
	Yes	No

	(n = 758) n (%)	(n = 33,775) n (%)	OR (99% CI)	AOR[a] (99% CI)	AOR[b] (99% CI)
Any substance use disorder	714 (94.2)	14090 (41.7)	**22.67 (15.18-33.86)**	**23.17 (15.45-34.74)**	**16.48 (10.94-24.83)**
Alcohol use disorder	695 (91.7)	11100 (32.9)	**22.54 (16.04-31.67)**	**24.56 (17.38-34.72)**	**13.59 (9.48-19.48)**
Alcohol abuse	209 (27.6)	7424 (22.0)	**1.35 (1.09-1.67)**	**1.29 (1.03-1.60)**	0.84 (0.67-1.06)
Alcohol dependence	514 (67.8)	4240 (12.6)	**14.67 (11.96-18.01)**	**15.04 (12.16-18.60)**	**8.01 (6.33-10.13)**
Drug use disorder	323 (42.6)	3646 (10.8)	**6.14 (5.05-7.45)**	**6.03 (4.93-7.39)**	**1.74 (1.40-2.17)**
Drug abuse	257 (33.9)	3219 (9.5)	**4.87 (3.97-5.97)**	**4.70 (3.80-5.81)**	**1.47 (1.17-1.84)**
Drug dependence	146 (19.3)	880 (2.6)	**8.92 (6.92-11.49)**	**8.08 (6.22-10.49)**	**2.02 (1.51-2.70)**
Nicotine dependence	394 (52.0)	6202 (18.4)	**4.81 (3.98-5.82)**	**4.58 (3.76-5.57)**	**1.60 (1.29-1.98)**
Any mood disorder	381 (50.3)	7086 (21.0)	**3.81 (3.15-4.60)**	**4.29 (3.53-5.21)**	**1.99 (1.59-2.48)**
Major depressive	300 (39.6)	6016 (17.8)	**3.02 (2.49-3.67)**	**3.52 (2.88-4.30)**	**1.61 (1.28-2.01)**
Dysthymia	133 (17.5)	1557 (4.6)	**4.40 (3.41-5.68)**	**4.85 (3.73-6.29)**	**2.05 (1.54-2.73)**
Mania	150 (19.8)	1117 (3.3)	**7.21 (5.63-9.24)**	**6.71 (5.21-8.66)**	**2.64 (1.99-3.51)**
Hypomania	47 (6.2)	848 (2.5)	**2.57 (1.72-3.82)**	**2.43 (1.62-3.64)**	1.22 (0.80-1.85)
Any anxiety disorder	282 (37.2)	6059 (17.9)	**2.71 (2.23-3.30)**	**3.07 (2.51-3.75)**	1.25 (0.99-1.57)
Panic only	93 (12.3)	1384 (4.1)	**3.27 (2.44-4.39)**	**3.62 (2.69-4.89)**	**1.56 (1.13-2.13)**
Panic + agoraphobia	40 (5.3)	376 (1.1)	**4.95 (3.19-7.68)**	**5.35 (3.42-8.37)**	**1.71 (1.07-2.75)**
Agoraphobia only	5 (0.7)	51 (0.2)	**4.39 (1.31-14.74)**	**4.17 (1.23-14.21)**	1.29 (0.37-4.50)
Social phobia	86 (11.3)	1671 (4.9)	**2.46 (1.82-3.33)**	**2.49 (1.83-3.37)**	0.91 (0.65-1.26)
Specific phobia	154 (20.3)	3352 (9.9)	**2.31 (1.83-2.93)**	**2.61 (2.05-3.32)**	1.23 (0.95-1.59)
Generalized anxiety	83 (10.9)	1462 (4.3)	**2.72 (2.00-3.70)**	**3.12 (2.28-4.27)**	1.02 (0.73-1.43)
Any personality disorder	351 (46.3)	5217 (15.4)	**4.72 (3.90-5.72)**	**4.50 (3.71-5.47)**	**2.20 (1.77-2.74)**
Histrionic	71 (9.4)	674 (2.0)	**5.08 (3.63-7.11)**	**4.80 (3.41-6.78)**	**1.98 (1.37-2.86)**
Antisocial	170 (22.4)	1182 (3.5)	**7.97 (6.29-10.10)**	**6.80 (5.31-8.70)**	**2.82 (2.18-3.66)**
Avoidant	69 (9.1)	774 (2.3)	**4.27 (3.04-5.99)**	**3.93 (2.78-5.55)**	**1.57 (1.07-2.28)**
Paranoid	142 (18.7)	1705 (5.0)	**4.34 (3.38-5.56)**	**4.04 (3.13-5.22)**	**1.77 (1.33-2.36)**
Schizoid	100 (13.2)	1131 (3.3)	**4.39 (3.29-5.85)**	**4.02 (3.00-5.37)**	**1.87 (1.37-2.56)**
Obsessive-compulsive	157 (20.7)	2723 (8.1)	**2.98 (2.35-3.77)**	**3.10 (2.44-3.94)**	**1.54 (1.19-2.00)**
Dependent	22 (2.9)	133 (0.4)	**7.56 (4.15-13.79)**	**6.33 (3.43-11.68)**	**2.19 (1.14-4.20)**
Psychotic disorders	44 (5.8)	278 (0.8)	**7.43 (4.83-11.41)**	**6.29 (4.06-9.75)**	**2.10 (1.31-3.36)**
Pathological gambling	25 (3.3)	160 (0.5)	**7.17 (4.08-12.57)**	**6.12 (3.46-10.84)**	**2.01 (1.11-3.63)**

Abbreviations: OR, odds ratio; AOR, adjusted odds ratio; CI, confidence interval. Bold font indicates statistical significance.

[a] Adjusted for demographic variables (gender, race, age, education, marital status, and personal income)

[b] Adjusted for demographic variables (gender, race, age, education, marital status, and personal income) and psychiatric disorders (any substance use disorder, any mood disorder, any anxiety disorder, and any personality disorder) unless the covariate of interest was a same disorder. Thus, each mood disorder was adjusted for any substance use disorder, any anxiety disorder, and any personality disorder. Each anxiety disorder was adjusted for any substance use disorder, any mood disorder, and any personality disorder. Each personality disorder was adjusted for any substance use disorder, any mood disorder, and any anxiety disorder. Each substance use disorder was adjusted for any mood disorder, any anxiety disorder, any personality disorder, and all other substance use disorders (except the same substance abuse/dependence).

Highlights

The epidemiology of Alcohol Withdrawal Hallucinations (AWH) suggests that age, higher educational attainment, and higher standard of living may act as protective factors against AWH; while social isolation, hypervigilance, exposure to alcohol during brain development, alcohol tolerance, and long and severe exposure to alcohol may increase risk for AWH.